

WHAT IS CLAIMED IS:

1 1. A compound that binds to a cysteine residue in the RNA-dependent
2 RNA polymerase (RdRp) protein of a virus forming a covalent bond.

1 2. A compound of Claim 1, wherein said RdRp protein is NS5B.

1 3. A compound of Claim 1, wherein said virus is hepatitis C virus
2 (HCV).

1 4. A compound of Claim 1, wherein said cysteine residue corresponds
2 to cysteine 366 in HCV NS5B.

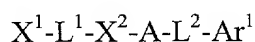
3 5. A compound of Claim 1, wherein said RdRp is NS5B and said
4 virus is HCV.

1 6. A compound of claim 5, wherein said covalent bond is irreversible
2 under physiological conditions.

1 7. A compound of claim 5, wherein said covalent bond is reversible
2 under physiological conditions.

1 8. A compound of claim 1, wherein said covalent bond results from a
2 reaction selected from the group consisting of a Michael addition of said cysteine residue
3 to an activated double or triple bond in said compound, an aromatic or aliphatic
4 nucleophilic substitution reaction of said cysteine residue with an electrophilic center in
5 said compound, a thioester forming reaction between said cysteine residue and a
6 carboxylic acid or carboxylic acid derivative in said compound, a disulfide forming
7 reaction between said cysteine residue and a sulfur-containing group in said compound,
8 and a hemi-thioketal forming reaction between said cysteine residue and an activated or
9 unactivated carbonyl group in said compound.

1 9. A compound useful for the covalent modification of a viral RNA-
2 dependent RNA polymerase (RdRp) protein, said compound having the formula (I):



4 wherein

A is a electrophilic group that reacts with a cysteine residue of said RdRp protein;

Ar^1 is a member selected from the group consisting of substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl;

X^1 is a member selected from the group consisting of -H, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, -CN, -CO₂H, -SO₃H, -C(O)NHOH, -NH₂, -OH, -NH(lower alkyl), -O(lower alkyl), -N(lower alkyl)₂, and -C(O)-NH(3-tetrazolyl);

L^1 is a divalent linking group selected from the group consisting of -CH₂CH₂-, -CH=CH-, -C≡C-, -O-, -S(O)_n-, -N(R_a)-, -C(O)-, -C(O)O-, -SO₂N(R_a)-, -CON(R_a)-, -N(R_a)CON(R_b)-, -N(R_a)N(R_b)-, -N(R_a)SO₂N(R_b)-, -N(R_a)SO₂-, -N(R_a)-O-, =N-O-, lower alkylene, -O-lower alkylene, -S(O)_n-lower alkylene, N(R_a)-lower alkylene, -SO₂N(R_a)-lower alkylene, lower alkylene-SO₂N(R_a)-, -CON(R_a)-lower alkylene, lower alkylene-CON(R_a)-, -N(R_a)CON(R_b)-lower alkylene, lower alkylene-N(R_a)N(R_b)-, -N(R_a)SO₂N(R_b)-lower alkylene, -N(R_a)-O-lower alkylene, lower alkylene-N(R_a)-O-, =N-O-lower alkylene, lower heteroalkylene, -O-lower heteroalkylene, -S(O)_n-lower heteroalkylene, N(R_a)-lower heteroalkylene, -SO₂N(R_a)-lower heteroalkylene, lower heteroalkylene-SO₂N(R_a)-, -CON(R_a)-lower heteroalkylene, lower heteroalkylene-CON(R_a)-, -N(R_a)CON(R_b)-lower heteroalkylene, lower heteroalkylene-N(R_a)N(R_b)-, -N(R_a)SO₂N(R_b)-lower heteroalkylene, -N(R_a)-O-lower heteroalkylene, lower heteroalkylene-N(R_a)-O-, =N-O-lower alkylene, aryl and heteroaryl;

X^2 is a member selected from the group consisting of substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, and substituted or unsubstituted heterocycloalkyl;

L^2 is a divalent linking group selected from the group consisting of -CH₂CH₂-, -(C(R_e)=C(R_d))_m-, -O-, -S(O)_n-, -N(R_e)-, -C(O)-, -C(O)O-, -SO₂N(R_e)-, -CON(R_e)-, -N(R_e)CON(R_f)-, -N(R_e)N(R_f)-, -N(R_e)SO₂N(R_f)-, -N(R_e)-O-, =N-O-, lower alkylene, perfluoro lower alkylene, polyfluoro lower alkylene, -O-lower alkylene, -S(O)_n-lower alkylene, N(R_e)-lower alkylene, -SO₂N(R_e)-lower alkylene, lower alkylene-SO₂N(R_e)-, -CON(R_e)-lower alkylene, lower alkylene-CON(R_e)-, -N(R_e)CON(R_f)-lower alkylene, lower alkylene-N(R_e)N(R_f)-, -N(R_e)SO₂N(R_f)-lower alkylene, -N(R_e)-O-lower alkylene, lower alkylene-N(R_e)-O-, =N-O-lower alkylene,

lower heteroalkylene, -O-lower heteroalkylene, -S(O)_n-lower heteroalkylene, N(R_e)-lower heteroalkylene, -SO₂N(R_e)-lower heteroalkylene, lower heteroalkylene-SO₂N(R_e)-, -CON(R_e)-lower heteroalkylene, lower heteroalkylene-CON(R_e)-, -N(R_e)CON(R_f)-lower heteroalkylene, lower heteroalkylene-N(R_e)N(R_f)-, -N(R_e)SO₂N(R_f)-lower heteroalkylene, -N(R_e)-O-lower heteroalkylene, lower heteroalkylene-N(R_e)-O-, =N-O-lower alkylene, aryl and heteroaryl, wherein R_a, R_b, R_c, R_d, R_e and R_f are each members independently selected from the group consisting of H, lower alkyl, lower heteroalkyl, -C(O)-lower alkyl, -C(O)-lower heteroalkyl, -S(O)₂-lower alkyl, and -S(O)₂-lower heteroalkyl;

the subscript n is an integer of from 0 to 2;

the subscript m is an integer of from 0 to 3;

the bond between X² and A can be a single, double or triple bond, depending on the nature of X² and A; and

wherein when L¹ and L² may be linked together *via* a single bond, -O-, -S- or amide group to form a new 5 to 7 membered ring; with the proviso that when A is an sp²-hybridized carbon atom and X² is substituted or unsubstituted rhodanine, L¹ is not -CH₂-CH₂-, -CH=CH-, -C≡C- or aryl.

10. A compound in accordance with claim 9, wherein

X² is selected from the group consisting of a 5 to 7 membered cycloalkyl ring, a 5 to 7 membered heterocycloalkyl ring containing from 1 to 3 heteroatoms, an aryl group and a heteroaryl group;

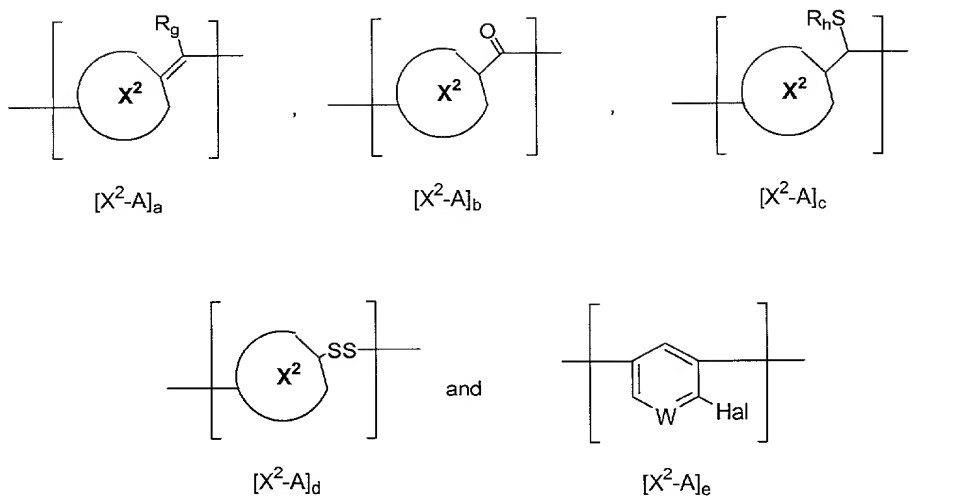
A is selected from the group consisting of an sp²-hybridized carbon atom and an sp³-hybridized carbon atom;

L² is a single bond; and

X² and A are joined *via* a single or double bond.

11. A compound in accordance with claim 10, wherein

X²-A- is selected from the group consisting of:

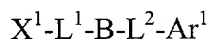


wherein R_g is selected from the group consisting of H, lower alkyl, lower alkoxy and F; R_h is selected from the group consisting of H, $-S(O)_n$ -lower alkyl, $-S(O)_n$ -lower heteroalkyl, $-S(O)_n$ -aryl and $-S(O)_n$ -heteroaryl;

W is CH or N; Hal is a halogen atom; and

X^2 is a substituted or unsubstituted member selected from the group consisting of a 5-6 membered cycloalkyl, 5-6 membered heterocycloalkyl containing from 1 to 3 heteroatoms, heteroaryl containing from 1 to 3 heteroatoms and aryl.

12. A compound having the formula (II):



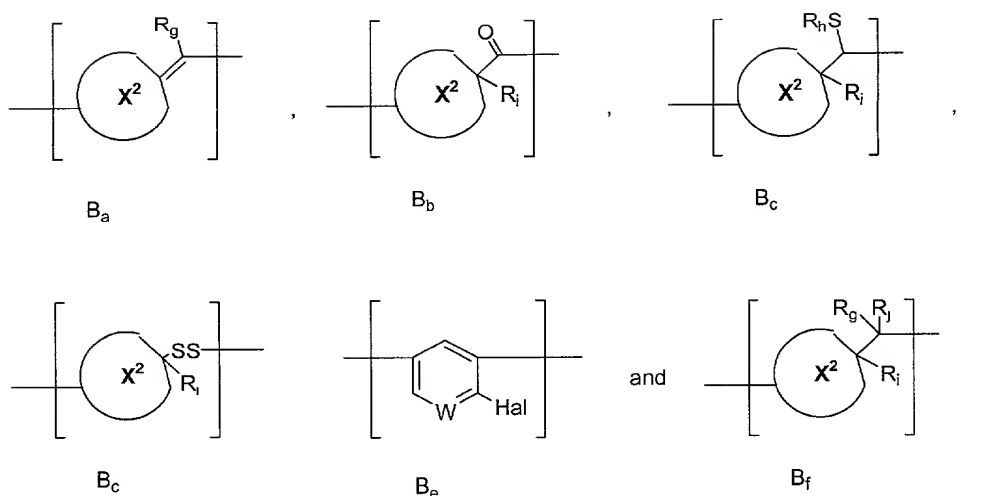
wherein

Ar^1 is a member selected from the group consisting of substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl;

X^1 is a member selected from the group consisting of -H, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, -CN, $-CO_2H$, $-SO_3H$, $-C(O)NHOH$, $-NH_2$, -OH, $-NH$ (lower alkyl), $-O$ (lower alkyl), $-N$ (lower alkyl)₂, and $-C(O)-NH$ (3-tetrazolyl);

L^1 is a divalent linking group selected from the group consisting of $-CH_2CH_2-$, $-CH=CH-$, $-C\equiv C-$, $-O-$, $-S(O)_n-$, $-N(R_a)-$, $-C(O)-$, $-C(O)O-$, $-SO_2N(R_a)-$, $-CON(R_a)-$, $-N(R_a)CON(R_b)-$, $-N(R_a)N(R_b)-$, $-N(R_a)SO_2N(R_b)-$, $-N(R_a)SO_2-$, $-N(R_a)-O-$, $=N-O-$, lower alkylene, $-O$ -lower alkylene, $-S(O)_n$ -lower alkylene, $N(R_a)$ -lower alkylene, $-SO_2N(R_a)$ -lower alkylene, lower alkylene- $SO_2N(R_a)-$, $-CON(R_a)$ -lower alkylene, lower alkylene- $CON(R_a)-$, $-N(R_a)CON(R_b)$ -lower alkylene, lower alkylene- $N(R_a)N(R_b)-$, $-N(R_a)SO_2N(R_b)$ -lower alkylene, $-N(R_a)-O$ -lower alkylene, lower alkylene- $N(R_a)-O-$,

- 17 =N-O-lower alkylene, lower heteroalkylene, -O-lower heteroalkylene, -S(O)_n-lower
- 18 heteroalkylene, N(R_a)-lower heteroalkylene, -SO₂N(R_a)-lower heteroalkylene, lower
- 19 heteroalkylene-SO₂N(R_a)-, -CON(R_a)-lower heteroalkylene, lower
- 20 heteroalkylene-CON(R_a)-, -N(R_a)CON(R_b)-lower heteroalkylene, lower
- 21 heteroalkylene-N(R_a)N(R_b)-, -N(R_a)SO₂N(R_b)-lower heteroalkylene, -N(R_a)-O-lower
- 22 heteroalkylene, lower heteroalkylene-N(R_a)-O-, =N-O-lower alkylene, aryl and
- 23 heteroaryl;
- 24 L² is a divalent linking group selected from the group consisting of
- 25 -CH₂CH₂-, -(C(R_c)=C(R_d))_m-, -O-, -S(O)_n-, -N(R_e)-, -C(O)-, -C(O)O-, -SO₂N(R_e)-,
- 26 -CON(R_e)-, -N(R_e)CON(R_f)-, -N(R_e)N(R_f)-, -N(R_e)SO₂N(R_f)-, -N(R_e)-O-, =N-O-, lower
- 27 alkylene, perfluoro lower alkylene, polyfluoro lower alkylene, -O-lower alkylene,
- 28 -S(O)_n-lower alkylene, N(R_e)-lower alkylene, -SO₂N(R_e)-lower alkylene, lower
- 29 alkylene-SO₂N(R_e)-, -CON(R_e)-lower alkylene, lower alkylene-CON(R_e)-,
- 30 -N(R_e)CON(R_f)-lower alkylene, lower alkylene-N(R_e)N(R_f)-, -N(R_e)SO₂N(R_f)-lower
- 31 alkylene, -N(R_e)-O-lower alkylene, lower alkylene-N(R_e)-O-, =N-O-lower alkylene,
- 32 lower heteroalkylene, -O-lower heteroalkylene, -S(O)_n-lower heteroalkylene, N(R_e)-lower
- 33 heteroalkylene, -SO₂N(R_e)-lower heteroalkylene, lower heteroalkylene-SO₂N(R_e)-,
- 34 -CON(R_e)-lower heteroalkylene, lower heteroalkylene-CON(R_e)-, -N(R_e)CON(R_f)-lower
- 35 heteroalkylene, lower heteroalkylene-N(R_e)N(R_f)-, -N(R_e)SO₂N(R_f)-lower
- 36 heteroalkylene, -N(R_e)-O-lower heteroalkylene, lower heteroalkylene-N(R_e)-O-,
- 37 =N-O-lower alkylene, aryl and heteroaryl, wherein R_a, R_b, R_c, R_d, R_e and R_f are each
- 38 members independently selected from the group consisting of H, lower alkyl, lower
- 39 heteroalkyl, -C(O)-lower alkyl, -C(O)-lower heteroalkyl, -S(O)₂-lower alkyl, and -
- 40 S(O)₂-lower heteroalkyl;
- 41 the subscript n is an integer of from 0 to 2;
- 42 the subscript m is an integer of from 0 to 3;
- 43 B is selected from the group consisting of:



wherein X^2 is a substituted or unsubstituted member selected from the group consisting of a 5-6 membered cycloalkyl, 5-6 membered heterocycloalkyl containing from 1 to 3 heteroatoms, heteroaryl containing from 1 to 3 heteroatoms and aryl;

W is CH or N;

R_g is selected from the group consisting of H, lower alkyl, lower alkoxy and F;

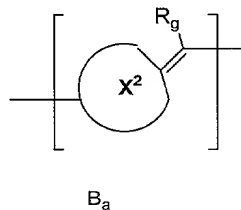
R_h is selected from the group consisting of H, $-S(O)_n$ -lower alkyl, $-S(O)_n$ -lower heteroalkyl, $-S(O)_n$ -aryl and $-S(O)_n$ -heteroaryl;

R_i is selected from the group consisting of H, lower alkyl, lower heteroalkyl, or a bond that links the atom bearing R_i with another atom in the X^2 ring;

R_j is selected from the group consisting of H, lower alkyl, F and lower alkoxy; and

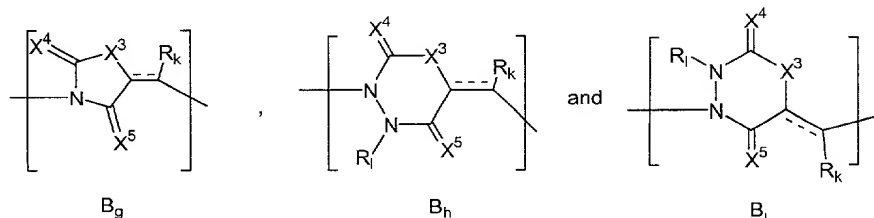
Hal is a halogen atom;

wherein when L^1 and L^2 may be linked together *via* a single bond, -O-, -S- or amide group to form a new 5 to 7 membered ring; with the proviso that when B is



65 and X^2 is rhodanine, L^1 is not $-\text{CH}_2-\text{CH}_2-$, $-\text{CH}=\text{CH}-$, $-\text{C}\equiv\text{C}-$ or aryl.

1 **13.** A compound in accordance with claim 12, wherein B is selected
2 from the group consisting of:



4 wherein

5 R_k is selected from the group consisting of H, lower alkyl, lower
6 heteroalkyl and F;

7 R_l is H or lower alkyl;

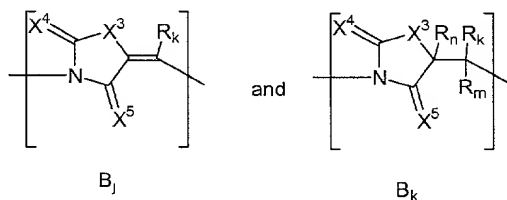
8 X^3 is selected from the group consisting of O, S, CH_2 , $\text{CH}(\text{lower alkyl})$,
9 $\text{C}(\text{lower alkyl})_2$, NH and $\text{N}(\text{lower alkyl})$;

10 X^4 is selected from the group consisting of O, S, NH and $\text{N}(\text{lower alkyl})$,
11 or X^4 and the carbon atom to which it is attached represents an sp^3 -hybridized carbon
12 having two substituents independently selected from the group consisting of H, lower
13 alkyl and lower heteroalkyl;

14 X^5 is selected from the group consisting of O, S, NH and $\text{N}(\text{lower alkyl})$,
15 or X^5 and the carbon atom to which it is attached represents an sp^3 -hybridized carbon
16 having two substituents independently selected from the group consisting of H, lower
17 alkyl, lower alkoxy, aryloxy, lower thioalkoxy and arylthioxy; and

18 $---$ represents either a single or double bond, with the proviso that when a
19 single bond is intended, the ring atom bearing said single bond bears an additional
20 substituent selected from the group consisting of H, lower alkyl, lower alkoxy and F.

1 **14.** A compound of claim 13, wherein B is selected from the group
2 consisting of:



4 wherein

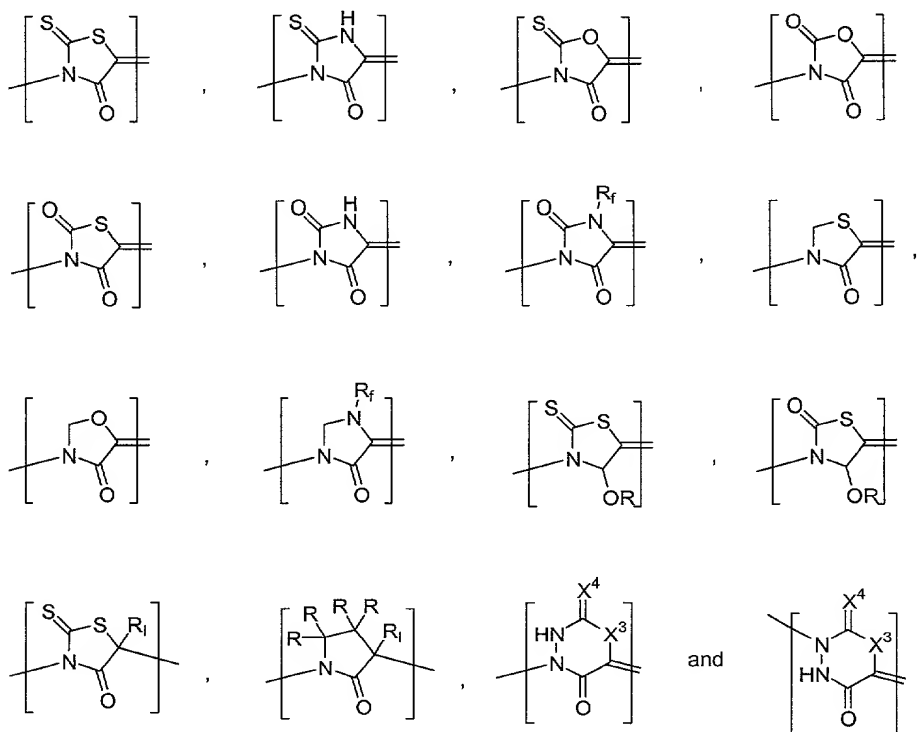
R_k, R_m and R_n are each independently selected from the group consisting of H, F, lower alkyl and lower alkoxy;

X³ is selected from the group consisting of O, S, C(lower alkyl)₂, NH and N(lower alkyl);

X⁴ is selected from the group consisting of O and S, or X⁴ and the carbon atom to which it is attached represents an sp³-hybridized carbon having two substituents independently selected from the group consisting of H, lower alkyl and lower heteroalkyl;

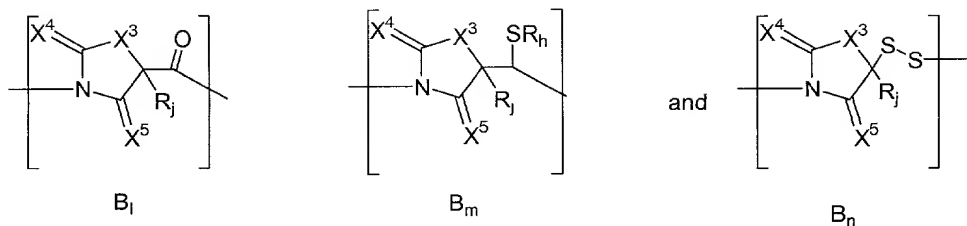
X⁵ is selected from the group consisting of O and S, or X⁵ and the carbon atom to which it is attached represents an sp³-hybridized carbon having two substituents independently selected from the group consisting of H, lower alkoxy and lower thioalkoxy.

15. A compound of claim 14, wherein B is selected from the group consisting of:



wherein any unlabeled R groups are independently selected from the group consisting of H, lower alkyl, lower alkoxy and F.

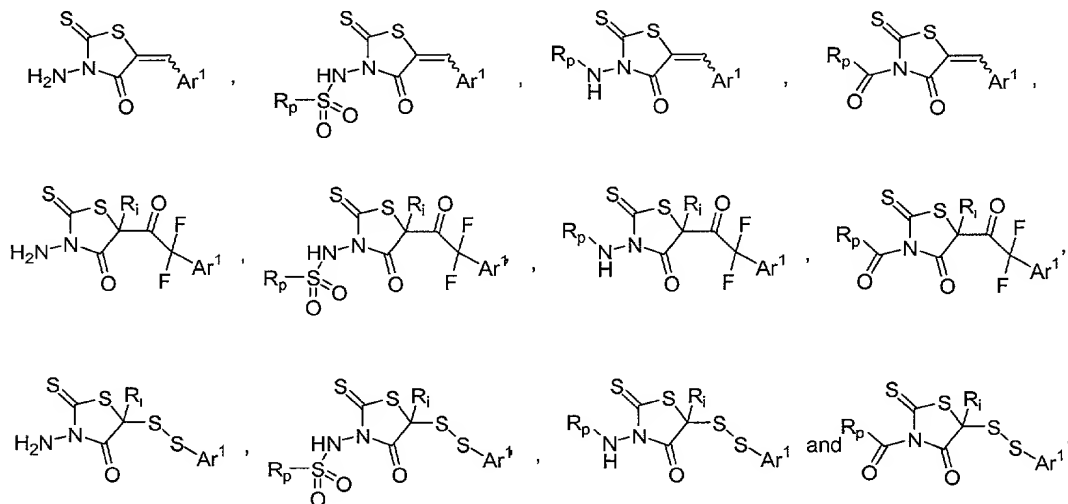
16. A compound of claim 12 wherein B is selected from the group consisting of:



17. A compound of claim 12, wherein L^1 is selected from the group consisting of $-\text{N}(\text{R}_a)-$, $-\text{N}(\text{R}_a)\text{-alkylene}$, $\text{alkylene-SO}_2\text{-N}(\text{R}_a)-$, $-\text{SO}_2\text{-N}(\text{R}_a)-$ and $-\text{N}(\text{R}_a)\text{SO}_2-$; and X^1 is selected from the group consisting of H, aryl and alkyl.

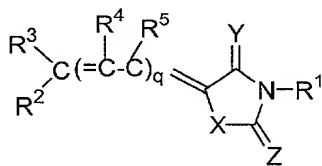
18. A compound of claim 12, wherein Ar^1 is selected from the group consisting of substituted or unsubstituted biphenyl group, substituted or unsubstituted bicyclic ring, substituted or unsubstituted phenyl group and substituted or unsubstituted pyridyl.

19. A compound of claim 17, said compound having the formula:



wherein R_p is selected from the group consisting of substituted or unsubstituted alkyl, substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl.

20. A compound of Claim 12, said compound having the formula (III):

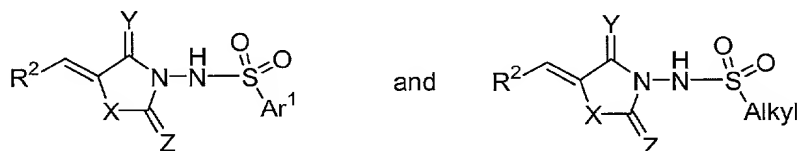


wherein

the subscript q is an integer of from 0 to 4;

11 C₈)alkoxy, phenoxy, phenyl(C₁-C₈)alkoxy, (C₁-C₈)acyl, (C₁-C₈)acyloxy, cyano,
 12 carbalkoxy, thio, (C₁-C₈)alkylthio, (C₁-C₈)alkylsulfinyl, (C₁-C₈)alkylsulfonyl, amino, (C₁-
 13 C₈)alkylamino, di(C₁-C₈)alkylamino, sulfonamido, carboxamido and (C₁-
 14 C₈)alkanoylamino.

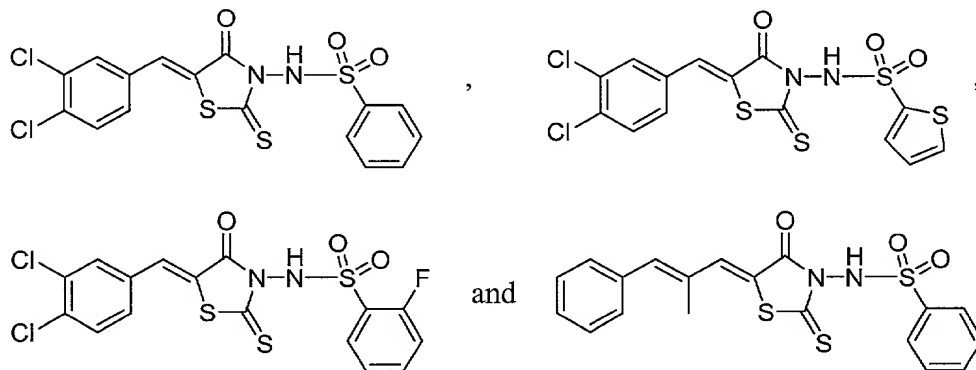
1 **22.** A compound of Claim 12, said compound having a formula
 2 selected from the group consisting of



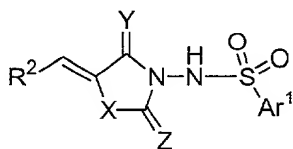
4 wherein

5 R² is a substituted or unsubstituted mono- or bi-heterocyclic group, a
 6 substituted or unsubstituted polycyclic ring, a substituted or unsubstituted alicyclic group
 7 having 5-8 carbon atoms, a substituted or unsubstituted phenyl group, a substituted or
 8 unsubstituted biphenyl group, a substituted or unsubstituted phenylether group, a
 9 substituted or unsubstituted cinnameryl group, or a substituted or unsubstituted stilbenyl
 10 group.

1 **23.** The compound of Claim 22, wherein said compound is selected
 2 from the group consisting of



1 **24.** A compound having the formula (**VIIa**):



wherein

Ar^1 is selected from the group consisting of substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl;

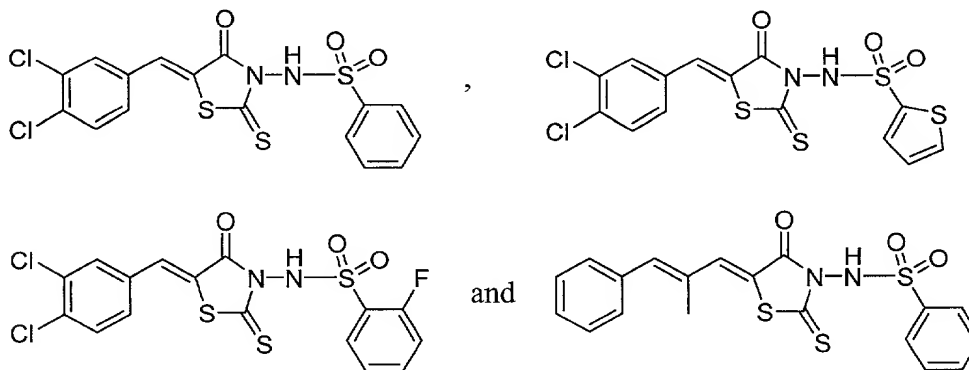
X is selected from $-\text{S}-$, $-\text{O}-$ and $-\text{N}(\text{R}_o)-$, wherein R_o is H or lower alkyl;

Y is O or S; and

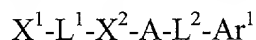
Z is O, S or $\text{N}(\text{R}_{2d})$, wherein R_{2d} is H or lower alkyl, or R_{2d} and R^1 may be joined to form an imidazole or benzimidazole group; and

R^2 is a substituted or unsubstituted mono- or bi-heterocyclic group, a substituted or unsubstituted polycyclic ring, a substituted or unsubstituted alicyclic group having 5-8 carbon atoms, a substituted or unsubstituted phenyl group, a substituted or unsubstituted biphenyl group, a substituted or unsubstituted phenylether group, a substituted or unsubstituted cinnameryl group, or a substituted or unsubstituted stilbenyl group.

25. The compound of Claim 24, wherein said compound is selected from the group consisting of



26. A compound useful for the covalent modification of a viral RNA-dependent RNA polymerase (RdRp) protein, said compound having the formula:



wherein

A is an electrophilic group that reacts with a cysteine residue of said viral RNA-dependent RNA polymerase protein;

Ar^1 is a member selected from the group consisting of substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl;

X^1 is a member selected from the group consisting of -H, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, -CN, -CO₂H, -SO₃H, -C(O)NHOH, -NH₂, -OH, -NH(lower alkyl), -O(lower alkyl), -N(lower alkyl)₂, and -C(O)-NH(3-tetrazolyl);

L^1 is a divalent linking group selected from the group consisting of -O-, -S(O)_n-, -N(R_a)-, -C(O)-, -C(O)O-, -SO₂N(R_a)-, -CON(R_a)-, -N(R_a)CON(R_b)-, -N(R_a)N(R_b)-, -N(R_a)SO₂N(R_b)-, -N(R_a)SO₂-, -N(R_a)-O-, =N-O-, lower alkylene, -O-lower alkylene, -S(O)_n-lower alkylene, N(R_a)-lower alkylene, -SO₂N(R_a)-lower alkylene, lower alkylene-SO₂N(R_a)-, -CON(R_a)-lower alkylene, lower alkylene-CON(R_a)-, -N(R_a)CON(R_b)-lower alkylene, lower alkylene-N(R_a)N(R_b)-, -N(R_a)SO₂N(R_b)-lower alkylene, -N(R_a)-O-lower alkylene, lower alkylene-N(R_a)-O-, =N-O-lower alkylene, lower heteroalkylene, -O-lower heteroalkylene, -S(O)_n-lower heteroalkylene, N(R_a)-lower heteroalkylene, -SO₂N(R_a)-lower heteroalkylene, lower heteroalkylene-SO₂N(R_a)-, -CON(R_a)-lower heteroalkylene, lower heteroalkylene-CON(R_a)-, -N(R_a)CON(R_b)-lower heteroalkylene, lower heteroalkylene-N(R_a)N(R_b)-, -N(R_a)SO₂N(R_b)-lower heteroalkylene, -N(R_a)-O-lower heteroalkylene, lower heteroalkylene-N(R_a)-O-, =N-O-lower alkylene and heteroaryl;

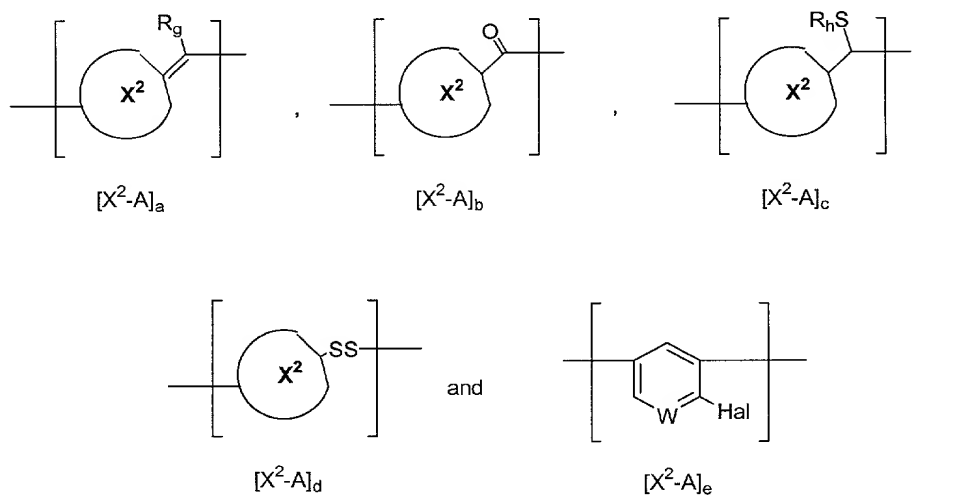
X^2 is a member selected from the group consisting of substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, and substituted or unsubstituted heterocycloalkyl;

L^2 is a divalent linking group selected from the group consisting of -CH₂CH₂-, -(C(R_c)=C(R_d))_m-, -O-, -S(O)_n-, -N(R_e)-, -C(O)-, -C(O)O-, -SO₂N(R_e)-, -CON(R_e)-, -N(R_e)CON(R_f)-, -N(R_e)N(R_f)-, -N(R_e)SO₂N(R_f)-, -N(R_e)-O-, =N-O-, lower alkylene, perfluoro lower alkylene, polyfluoro lower alkylene, -O-lower alkylene, -S(O)_n-lower alkylene, N(R_e)-lower alkylene, -SO₂N(R_e)-lower alkylene, lower alkylene-SO₂N(R_e)-, -CON(R_e)-lower alkylene, lower alkylene-CON(R_e)-, -N(R_e)CON(R_f)-lower alkylene, lower alkylene-N(R_e)N(R_f)-, -N(R_e)SO₂N(R_f)-lower alkylene, -N(R_e)-O-lower alkylene, lower alkylene-N(R_e)-O-, =N-O-lower alkylene, lower heteroalkylene, -O-lower heteroalkylene, -S(O)_n-lower heteroalkylene, N(R_e)-lower heteroalkylene, -SO₂N(R_e)-lower heteroalkylene, lower heteroalkylene-SO₂N(R_e)-, -CON(R_e)-lower heteroalkylene, lower heteroalkylene-CON(R_e)-, -N(R_e)CON(R_f)-lower heteroalkylene, lower heteroalkylene-N(R_e)N(R_f)-, -N(R_e)SO₂N(R_f)-lower heteroalkylene, -N(R_e)-O-lower heteroalkylene, lower heteroalkylene-N(R_e)-O-, =N-O-lower alkylene, aryl and heteroaryl;

wherein R_a , R_b , R_c , R_d , R_e and R_f are each members independently selected from the group consisting of H, lower alkyl, lower heteroalkyl, $-C(O)$ -lower alkyl, $-C(O)$ -lower heteroalkyl, $-S(O)_2$ -lower alkyl, and $-S(O)_2$ -lower heteroalkyl; the subscript n is an integer of from 0 to 2; the subscript m is an integer of from 0 to 3; the bond between X^2 and A can be a single, double or triple bond, depending on the nature of X^2 and A; and wherein when L^1 and L^2 may be linked together *via* a single bond, $-O-$, $-S-$ or amide group to form a new 5 to 7 membered ring.

27. A compound in accordance with claim **26**, wherein X^2 is selected from the group consisting of a 5 to 7 membered cycloalkyl ring, a 5 to 7 membered heterocycloalkyl ring containing from 1 to 3 heteroatoms, an aryl group and a heteroaryl group; A is selected from the group consisting of an sp^2 -hybridized carbon atom and an sp^3 -hybridized carbon atom; L^2 is a single bond; and X^2 and A are joined *via* a single or double bond.

28. A compound in accordance with claim **27**, wherein $-X^2-A-$ is selected from the group consisting of:



wherein R_g is selected from the group consisting of H, lower alkyl, lower alkoxy and F;

R_h is selected from the group consisting of H, $-S(O)_n$ -lower alkyl, $-S(O)_n$ -lower heteroalkyl, $-S(O)_n$ -aryl and $-S(O)_n$ -heteroaryl; W is CH or N; Hal is a halogen atom; and X^2 is a substituted or unsubstituted member selected from the group consisting

9 of a 5-6 membered cycloalkyl, 5-6 membered heterocycloalkyl containing from 1 to 3
 10 heteroatoms, heteroaryl containing from 1 to 3 heteroatoms and aryl.

1 **29.** A compound having the formula (II):



3 wherein

4 Ar^1 is a member selected from the group consisting of substituted or
 5 unsubstituted aryl and substituted or unsubstituted heteroaryl;

6 X^1 is a member selected from the group consisting of -H, substituted or
 7 unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted
 8 heteroaryl, -CN, -CO₂H, -SO₃H, -C(O)NHOH, -NH₂, -OH, -NH(lower alkyl), -O(lower
 9 alkyl), -N(lower alkyl)₂, and -C(O)-NH(3-tetrazolyl);

10 L^1 is a divalent linking group selected from the group consisting of -O-,
 11 -S(O)_n-, -N(R_a)-, -C(O)-, -C(O)O-, -SO₂N(R_a)-, -CON(R_a)-, -N(R_a)CON(R_b)-,
 12 -N(R_a)N(R_b)-, -N(R_a)SO₂N(R_b)-, -N(R_a)SO₂-, -N(R_a)-O-, =N-O-, lower alkylene,
 13 -O-lower alkylene, -S(O)_n-lower alkylene, N(R_a)-lower alkylene, -SO₂N(R_a)-lower
 14 alkylene, lower alkylene-SO₂N(R_a)-, -CON(R_a)-lower alkylene, lower
 15 alkylene-CON(R_a)-, -N(R_a)CON(R_b)-lower alkylene, lower alkylene-N(R_a)N(R_b)-,
 16 -N(R_a)SO₂N(R_b)-lower alkylene, -N(R_a)-O-lower alkylene, lower alkylene-N(R_a)-O-,
 17 =N-O-lower alkylene, lower heteroalkylene, -O-lower heteroalkylene, -S(O)_n-lower
 18 heteroalkylene, N(R_a)-lower heteroalkylene, -SO₂N(R_a)-lower heteroalkylene, lower
 19 heteroalkylene-SO₂N(R_a)-, -CON(R_a)-lower heteroalkylene, lower
 20 heteroalkylene-CON(R_a)-, -N(R_a)CON(R_b)-lower heteroalkylene, lower
 21 heteroalkylene-N(R_a)N(R_b)-, -N(R_a)SO₂N(R_b)-lower heteroalkylene, -N(R_a)-O-lower
 22 heteroalkylene, lower heteroalkylene-N(R_a)-O-, =N-O-lower alkylene and heteroaryl;

23 L^2 is a divalent linking group selected from the group consisting of
 24 -CH₂CH₂-, -(C(R_c)=C(R_d))_m-, -O-, -S(O)_n-, -N(R_e)-, -C(O)-, -C(O)O-, -SO₂N(R_e)-,
 25 -CON(R_e)-, -N(R_e)CON(R_f)-, -N(R_e)N(R_f)-, -N(R_e)SO₂N(R_f)-, -N(R_e)-O-, =N-O-, lower
 26 alkylene, perfluoro lower alkylene, polyfluoro lower alkylene, -O-lower alkylene,
 27 -S(O)_n-lower alkylene, N(R_e)-lower alkylene, -SO₂N(R_e)-lower alkylene, lower
 28 alkylene-SO₂N(R_e)-, -CON(R_e)-lower alkylene, lower alkylene-CON(R_e)-,
 29 -N(R_e)CON(R_f)-lower alkylene, lower alkylene-N(R_e)N(R_f)-, -N(R_e)SO₂N(R_f)-lower
 30 alkylene, -N(R_e)-O-lower alkylene, lower alkylene-N(R_e)-O-, =N-O-lower alkylene,

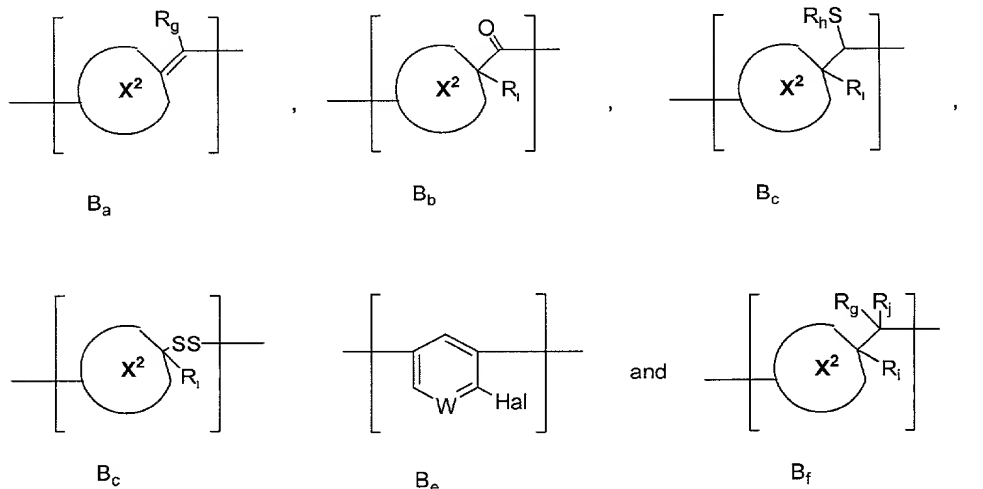
lower heteroalkylene, -O-lower heteroalkylene, -S(O)_n-lower heteroalkylene, N(R_e)-lower heteroalkylene, -SO₂N(R_e)-lower heteroalkylene, lower heteroalkylene-SO₂N(R_e)-, -CON(R_e)-lower heteroalkylene, lower heteroalkylene-CON(R_e)-, -N(R_e)CON(R_f)-lower heteroalkylene, lower heteroalkylene-N(R_e)N(R_f)-, -N(R_e)SO₂N(R_f)-lower heteroalkylene, -N(R_e)-O-lower heteroalkylene, lower heteroalkylene-N(R_e)-O-, =N-O-lower alkylene, aryl and heteroaryl;

wherein R_a, R_b, R_c, R_d, R_e and R_f are each members independently selected from the group consisting of H, lower alkyl, lower heteroalkyl, -C(O)-lower alkyl, -C(O)-lower heteroalkyl, -S(O)₂-lower alkyl, and -S(O)₂-lower heteroalkyl;

the subscript n is an integer of from 0 to 2;

the subscript m is an integer of from 0 to 3;

B is selected from the group consisting of:



wherein

X² is a substituted or unsubstituted member selected from the group consisting of a 5-6 membered cycloalkyl, 5-6 membered heterocycloalkyl containing from 1 to 3 heteroatoms, heteroaryl containing from 1 to 3 heteroatoms and aryl;

W is CH or N;

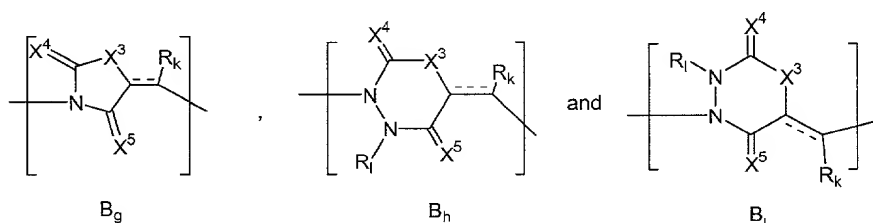
R_g is selected from the group consisting of H, lower alkyl, lower alkoxy and F;

R_h is selected from the group consisting of H, -S(O)_n-lower alkyl, -S(O)_n-lower heteroalkyl, -S(O)_n-aryl and -S(O)_n-heteroaryl;

R_i is selected from the group consisting of H, lower alkyl, lower heteroalkyl, or a bond that links the atom bearing R_i with another atom in the X² ring;

R_j is selected from the group consisting of H, lower alkyl, F and lower alkoxy; and
 Hal is a halogen atom;
 wherein when L^1 and L^2 may be linked together *via* a single bond, -O-, -S- or amide group to form a new 5 to 7 membered ring.

30. A compound in accordance with claim 29, wherein B is selected from the group consisting of:



wherein

R_k is selected from the group consisting of H, lower alkyl, lower heteroalkyl and F;

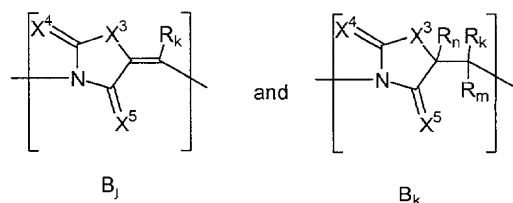
R_l is H or lower alkyl;

X^3 is selected from the group consisting of O, S, CH_2 , CH (lower alkyl), C (lower alkyl)₂, NH and N(lower alkyl);

X^4 is selected from the group consisting of O, S, NH and N(lower alkyl), or X^4 and the carbon atom to which it is attached represents an sp^3 -hybridized carbon having two substituents independently selected from the group consisting of H, lower alkyl and lower heteroalkyl; and

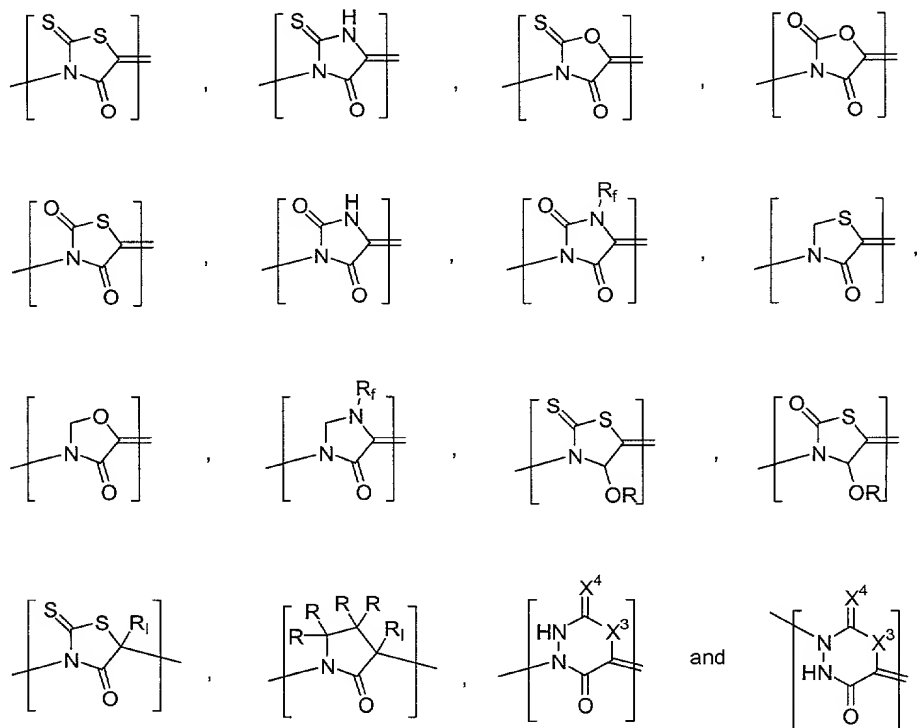
X^5 is selected from the group consisting of O, S, NH and N(lower alkyl), or X^5 and the carbon atom to which it is attached represents an sp^3 -hybridized carbon having two substituents independently selected from the group consisting of H, lower alkyl, lower alkoxy, aryloxy, lower thioalkoxy and arylthioxy; and $- - -$ represents either a single or double bond, with the proviso that when a single bond is intended, the ring atom bearing said single bond bears an additional substituent selected from the group consisting of H, lower alkyl, lower alkoxy and F.

31. A compound of claim 30, wherein B is selected from the group consisting of:



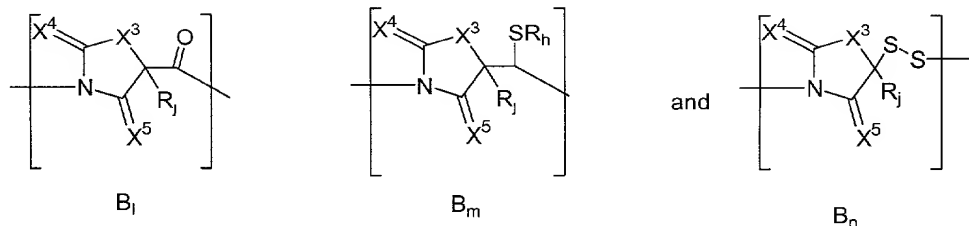
wherein R_k , R_m and R_n are each independently selected from the group consisting of H, F, lower alkyl and lower alkoxy; X^3 is selected from the group consisting of O, S, C(lower alkyl)₂, NH and N(lower alkyl); X^4 is selected from the group consisting of O, S, or X^4 and the carbon atom to which it is attached represents an sp^3 -hybridized carbon having two substituents independently selected from the group consisting of H, lower alkyl and lower heteroalkyl; X^5 is selected from the group consisting of O, S, or X^5 and the carbon atom to which it is attached represents an sp^3 -hybridized carbon having two substituents independently selected from the group consisting of H, lower alkoxy and lower thioalkoxy.

32. A compound of claim 31, wherein B is selected from the group consisting of:



wherein any unlabeled R groups are independently selected from the group consisting of H, lower alkyl, lower alkoxy and F.

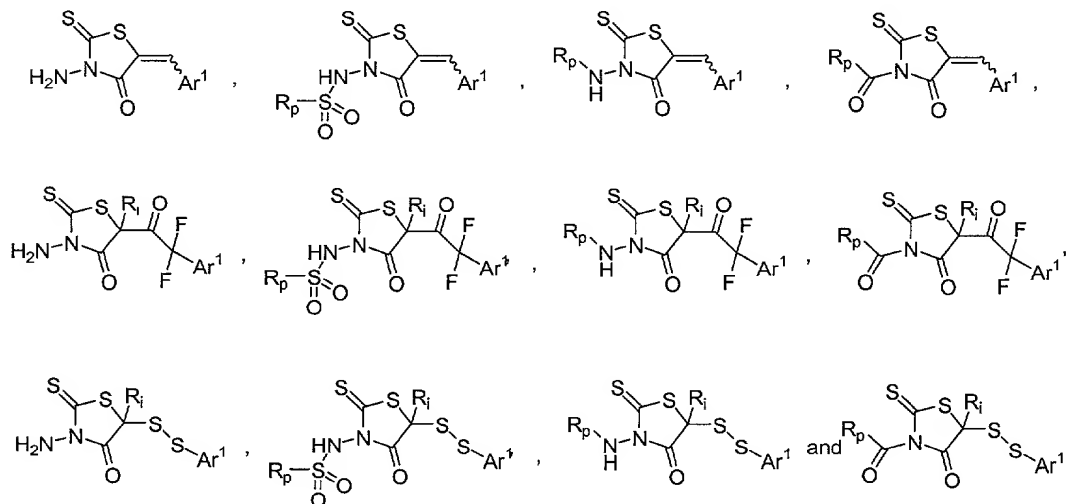
33. A compound of claim 29, wherein B is selected from the group consisting of:



34. A compound of claim 29 wherein L^1 is selected from the group consisting of $-N(R_a)-$, $-N(R_a)$ -alkylene, alkylene- $SO_2-N(R_a)-$, $-SO_2-N(R_a)-$ and $-N(R_a)SO_2-$; and X^1 is selected from the group consisting of H, aryl and alkyl.

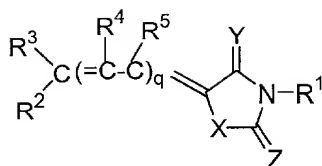
35. A compound of claim 29, wherein Ar^1 is selected from the group consisting of substituted or unsubstituted biphenyl group, substituted or unsubstituted bicyclic ring, substituted or unsubstituted phenyl group and substituted or unsubstituted pyridyl.

36. A compound of claim 34, said compound having the formula:



wherein R_p is a member selected from the group consisting of substituted or unsubstituted alkyl, substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl.

37. A compound of Claim 29, said compound having the formula (III):



wherein

the subscript q is an integer of from 0 to 4;

R¹ is hydrogen or a substituent having the formula -L¹-COOH;

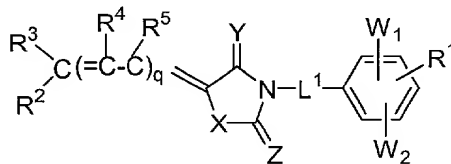
X is a moiety selected from -S-, -O-, and -N(R₀)-, wherein R₀ is H or lower alkyl;

R² is a substituted or unsubstituted aryl(C₁-C₈)alkyl, a substituted or unsubstituted aryl(C₁-C₈)alkenyl, a substituted or unsubstituted aryl(C₁-C₈)alkynyl, a substituted or unsubstituted alicyclic group having from 5-8 carbon atoms, or a group having the formula (R₂ₐ)ᵣ-(L)ₛ-R₂ᵇ, wherein R₂ₐ and R₂ᵇ can be the same or different and represent a substituted or unsubstituted heterocyclic group or a substituted or unsubstituted phenyl group, R₂ₐ can also represent a substituted or unsubstituted polycyclic group, and L represents a divalent linking group selected from methylene, ethylene, propylene, -CH=CH-, -C≡C-, -C(O)-, -O-, -S-, -S(O)-, -S(O)₂-, or -N(R₂c)-, wherein R₂c is selected from H or lower alkyl, and the subscripts r and s are each independently 0 or 1;

Y represents O or S; and

Z represents O, S or N(R₂d), wherein R₂d is H or lower alkyl, or R₂d and R¹ may be joined to form an imidazole or benzimidazole group; with the proviso that when R¹ is hydrogen R² is not substituted or unsubstituted furan.

38. A compound of Claim 29, said compound having the formula (V):

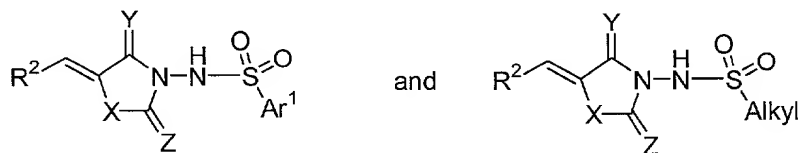


wherein

R¹ is H, -OH, -COORᵤ, -CONRᵥRᵂ, -SO₂NRₓRᵧ wherein Rᵤ, Rᵥ, Rᵂ, Rₓ and Rᵧ are H or lower alkyl, or R¹ is a mono-heterocyclic group selected from furan, thiophene, pyridine, pyrimidine, pyridazine, 1,3-oxathiolane, tetrazole, oxadiazole, oxazole, triazole, imidazoline, imidazole, thiazole, thiadiazole, pyrrole, piperidine, morpholine, triazine and pyrazole; and

9 W_1 and W_2 are independently selected from H, (C₁-C₈)alkyl, (C₁-
 10 C₈)alkenyl, (C₁-C₈)alkynyl, halogen, nitro, hydroxy, perfluoroalkyl, difluoromethyl, (C₁-
 11 C₈)alkoxy, phenoxy, phenyl(C₁-C₈)alkoxy, (C₁-C₈)acyl, (C₁-C₈)acyloxy, cyano,
 12 carbalkoxy, thio, (C₁-C₈)alkylthio, (C₁-C₈)alkylsulfinyl, (C₁-C₈)alkylsulfonyl, amino, (C₁-
 13 C₈)alkylamino, di(C₁-C₈)alkylamino, sulfonamido, carboxamido and (C₁-
 14 C₈)alkanoylamino.

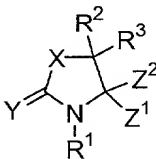
1 **39.** A compound of Claim 29, said compound having a formula
 2 selected from the group consisting of



3
 4 wherein

5 R^2 is a substituted or unsubstituted mono- or bi-heterocyclic group, a
 6 substituted or unsubstituted polycyclic ring, a substituted or unsubstituted alicyclic group
 7 having 5-8 carbon atoms, a substituted or unsubstituted phenyl group, a substituted or
 8 unsubstituted biphenyl group, a substituted or unsubstituted phenylether group, a
 9 substituted or unsubstituted cinnameryl group, or a substituted or unsubstituted stilbenyl
 10 group.

1 **40.** A compound having the formula:



2
 3 wherein

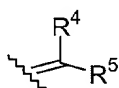
4 X is a member selected from the group consisting of O, S, NR¹¹ and
 5 CR¹¹R¹² wherein R¹¹ and R¹² are each members independently selected from the group
 6 consisting of H, substituted or unsubstituted (C₁-C₈)alkyl, substituted or unsubstituted
 7 (C₁-C₈)alkoxy and substituted or unsubstituted (C₁-C₈)acyl;

8 Y is a member selected from the group consisting of O and S, or taken
 9 together with the carbon atom to which it is attached forms a methylene group;

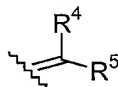
10 Z¹ and Z² are each members independently selected from the group
 11 consisting of H and substituted or unsubstituted (C₁-C₈)alkoxy, or taken together form an
 12 oxo moiety;

R¹ is a member selected from the group consisting of substituted or unsubstituted (C₁-C₈)alkyl, substituted or unsubstituted (C₁-C₈)alkylamino, substituted or unsubstituted di(C₁-C₈)alkylamino, substituted or unsubstituted (C₁-C₈)acylamino, amino, H, substituted or unsubstituted aryl(C₁-C₈)alkyl, substituted or unsubstituted heteroaryl(C₁-C₈)alkyl, substituted or unsubstituted heterocycloalkyl and -NHSO₂-Ar¹, wherein Ar¹ is selected from the group consisting of substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl; and

R² and R³ are each members independently selected from the group consisting of halo, substituted or unsubstituted (C₁-C₈)alkyl and substituted or unsubstituted (C₁-C₈)acyl, or taken together form a group of the formula:



wherein R⁴ and R⁵ are each members independently selected from the group consisting of H, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl, with the proviso that no more than one of R⁴ and R⁵ are H; with the proviso that when Z¹ and Z² taken together form an oxo moiety and R² and R³ taken together form a group of the formula:



R¹ is not substituted or unsubstituted (C₁-C₈)alkyl or H

41. A compound in accordance with claim 40, wherein R¹ is selected from the group consisting of amino and substituted or unsubstituted -NHSO₂-Ar¹.

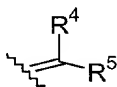
42. A compound in accordance with claim 40, wherein Z^1 and Z^2 taken together are oxo.

43. A compound in accordance with claim 40, wherein Y is O or S and Z¹ and Z² taken together are oxo.

44. A compound in accordance with claim **40**, wherein X and Y are S and Z¹ and Z² taken together are oxo.

45. A compound in accordance with claim **40**, wherein R¹ is selected from the group consisting of substituted or unsubstituted (C₁-C₈)alkylamino, substituted

or unsubstituted di(C₁-C₈)alkylamino, substituted or unsubstituted (C₁-C₈)acylamino, amino, and -NHSO₂-Ar¹, wherein Ar¹ is selected from the group consisting of substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl; X and Y are each independently selected from the group consisting of O and S; Z¹ and Z² taken together are oxo; and R² and R³ taken together are a group having the formula:



wherein R⁴ and R⁵ are each members independently selected from the group consisting of H, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl, with the proviso that only one of R⁴ and R⁵ is H.

46. A pharmaceutical composition, comprising a pharmaceutically acceptable carrier and a therapeutically or prophylactically effective amount of a compound of any one of claims 1, 9, 12, 24, 26, 29 and 40.

47. A method for the treatment or prevention of a viral infection, comprising administering to a subject suffering from or at risk for said viral infection an effective amount of a compound of any one of claims 1, 9, 12, 24, 26, 29 and 40.

48. The method of Claim 47, wherein said viral infection is hepatitis C virus infection.

49. The method of Claim 47, wherein said compound is administered in combination with a therapeutically effective amount of an antiviral agent.

50. The method of Claim 49, wherein said antiviral agent is an interferon.

51. A method for treating or preventing a viral infection, comprising administering to a subject in need thereof a therapeutically effective amount of a compound that binds to a cysteine residue in the RNA-dependent RNA polymerase (RdRp) protein of a virus forming a covalent bond.

52. The method of Claim 51, wherein said RdRp protein is NS5B.

1 **53.** The method of Claim **51**, wherein said viral infection is hepatitis C
2 virus infection.

1 **54.** The method of Claim **51**, wherein said compound comprises an
2 electrophilic group that reacts with a cysteine residue of said RdRp protein.

1 **55.** The method of Claim **54**, wherein said electrophilic group is
2 selected from the group consisting of an activated double or triple bond, an electrophilic
3 center, a carboxylic acid or carboxylic acid derivative, a sulfur-containing group and an
4 activated or unactivated carbonyl group.